DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-5, 10-14, 20-23 and 29-33, drawn to a method of sequencing a population of encoding antibodies, classified in class 435, subclass 6.

II. Claims 39, drawn to an oligonucleotide library, classified in class 536, subclass 23.1.

The inventions are distinct, each from the other because of the following reasons:

2. Inventions II and I are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case, the library of oligonucleotide can be used in a materially different method besides in the sequencing method via hybridization. For example, the library of oligonucleotides can be used in methods of nucleic acid cloning via amplification or in methods of differential mutagenesis or aptamer studies or in antisense studies. A search burden exists if the different inventions of groups I and II are searched together because the searches of the different inventions are not coextensive. Specifically, a search for a method of sequencing a population of polynucleotides encoding antibodies or T-cell receptors is not required for or is necessary for a search of an oligonucleotide library. Prior art which teaches the library of oligonucleotides may not have any knowledge of its use in

methods of sequencing a population of polynucleotides encoding antibodies or T-cell receptors. Additionally, even if the library of oligonucleotides was known, the use of the library in a method of sequencing may be novel and unobvious in view of the preamble and active steps.

3. Restriction for examination purposes as indicated is proper because all these inventions listed in this action are independent or distinct for the reasons given above and there would be a serious search and examination burden if restriction were not required because one or more of the following reasons apply:

(a) the inventions have acquired a separate status in the art in view of their different classification;

(b) the inventions have acquired a separate status in the art due to their recognized divergent subject matter;

(c) the inventions require a different field of search (for example, searching different classes/subclasses or electronic resources, or employing different search queries);

(d) the prior art applicable to one invention would not likely be applicable to another invention;

(e) the inventions are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a invention to be examined even though the requirement

may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected invention**.

The election of an invention may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected invention.

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Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

4. During a telephone conversation with Martin Moynihan on March 5, 2008 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-5, 10-14, 20-23, 29-33. Affirmation of this election must be made by applicant

in replying to this Office action. Claim 39 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Objections

6. Claim 1 is objected to because of the following informalities:

(a) The world "polynuclrotide" in line 2 is misspelled. Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-5, 10-14, 20-23, 29-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claims 1-5, 10-14, 20-23 and 29-33 are indefinite at in the step (a) of claims 1 and 20, because it is confusing and unclear as to which plurality of oligonucleotides are contacted together in order to form the hybridization duplexes. The step (a) does not set out with clarity the hybridization step.

(b) The claims 1-5, 10-14, 20-23, 29-33 are indefinite and vague at the recitation of "a quantum above a predetermined threshold, so as to define a population of positively hybridizing oligonucleotides" in the claims 1 and 20 at step (c)-(i) because neither the claims nor specification provides a prerequisite for the terms recited in the claims and it cannot be determine what conditions or requirements are necessary to determine a population of positively hybridizing oligonucleotides. Further, the steps (c)-(ii) and (c)-(iii) are vague and confusing because it is unclear as to what segment of the sequences are germline segments, what sequences are considered germline sequences, what method steps are required to identify germline sequences and how these sequences differ from any other sequence which hybridizes. The claims do not provide a clear nexus between the steps (a) and (b) and the compiling step (c). Clarification is required as to Applicant's intent.

(c) Claims 2 and 21 are vague at the recitation of non-redundant germline sequence because the term has not been defined in the specification and it cannot be determined what sequences are considered non-redundant germline sequences.

Claim Interpretation

The claims as currently written are extremely broad and thus a clear interpretation of Applicant's intent cannot be ascertained, especially at the step (c). Accordingly, for the purpose of application of prior art, the claims are being interpreted by the examiner as requiring a method of sequencing by hybridization of polynucleotides encoding antibodies or T-cell receptors. Additionally, neither the

specification nor claims provide a definition of a germline sequence, germline segment or non-redundant germline sequence. The specification at paragraph 0117 of the printed publication (20070161001) suggests that a germline sequence is "a specific sequence". Therefore, the terms germline sequence and germline segment are being interpreted by the Examiner as any specific target sequence. The term non-redundant germline sequence is being interpreted by the Examiner as any non-specific sequence.

The prior art rejections below are based on the Examiner's best interpretation of the claims.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Drmanac et al (Advances in Biochemical Engineering/Biotechnology, citation made of record in the IDS filed 6/26/2007). Regarding claim 1, Drmanac et al teach a method of sequencing a population of T-cell DNA fragments comprising contacting a plurality of oligonucleotides of known sequence with a population of T-cell DNA fragments under conditions which forms hybridization duplexes, wherein some of the plurality of oligonucleotides have a partial sequence which is similar to the population of T-cell DNA fragments and quantitatively detecting oligonucleotides involved in the formation of the

hybridization duplexes and compiling sets of sequences based on the hybridization profiles (see page 79-86 and 91, sections 2.1 through 3.2 and 4.6).

Regarding claim 11, Drmanac et al teach wherein the population of polynucleotides comprises DNA molecules (section 3.2).

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5, 10-14, 20-23, 29-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zang et al (WO 03059155, January 2002) in view of Drmanac as previously described above.

Regarding claims 1-5, 12-14, 20-23, and 31-33 Zang et al teach a method that can distinguish between various T-cell receptor V genes, said method comprising providing a population of polynucleotides encoding a T-cell receptor, contacting the population of polynucleotide encoding a T-cell receptor with a plurality of oligonucleotides of known sequence under conditions allowing a formation of hybridization between the plurality of oligonucleotides of know sequence and the population of polynucleotides encoding a T-cell receptor and quantitatively detecting oligonucleotides involved in said formation of said hybridization duplexes by determining the level of expression of the hybridization profiles (page 3, lines 19-27,

page 4, lines 17-18, 25-32 and pages 5-8). Zang et al further teach wherein the method comprises step of amplifying selected segments of said polynucleotides encoding the T-cell receptor (page 5) and wherein the segments of said polynucleotides include variable segments, diversity segments, junction segments and constant segments as ell as hypervariable complementary determining region-3 (CDR3) see page 1).

Zang et al do not expressly teach wherein the method teaches steps of compiling sequences based on overlapping hybridization profiles.

Drmanac et al teaches a method for sequencing a T-cell receptor gene by hybridization using a probe array. Drmanac et al teach wherein the method comprises providing a set of oligonucleotides which hybridizes under conditions that allow detection of complementary sequences in the target nucleic acid. Drmanac teaches that the sequencing methods involve a complete set of *n*-mers probes, each DNA bases is redundantly read by n overlapping probes. Drmanac teaches that this overlap principle allows determination of sequences that are much longer than the length of each probe by comparing and aligning n-1 or fewer overlapping bases that are shared by the probes. Drmanac teaches that the advantages of probe overlap are that the effect of random errors is minimized because each base is "read" by multiple probes. Drmanac teaches this process allows researchers to sequence mixture of fragments from different DNA molecules. (pages 79 and 80). Drmanac et al further teach that the sequencing method by hybridization is also useful for detecting mutations in a medically important gene or for detecting mutations in patient DNA sample (section 3.3

In view of the foregoing, one of ordinary skill in the art would have been motivated to further encompass a step of compiling sequences based on positive overlapping hybridization profiles in the method of Zang et al for the improved benefit of reducing random errors during sequence detection and/or mutation detection associated with a disease in a population of or mixture of different DNA molecules as suggested by Drmanac. One of ordinary skill in the art could predict a reasonable expectation of success using the SBH method of Drmanac in the gene array method of Zang et al.

Regarding claims 10 and 29, Zhang et al teach wherein the polynucleotides are RNA molecules (page 7).

Regarding claims 11 and 30, Drmanac et al teach wherein the polynucleotides are DNA molecules (section 3.2).

Conclusion

12. No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to CYNTHIA B. WILDER whose telephone number is (571)272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Cynthia B. Wilder/
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Art Unit 1637

4/9/2008